

Appl. No. 09/346,069

Amdt. dated

Reply to Final Office Action of May 3, 2004

This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1-14. (canceled)

15. (previously presented) The composition of matter of Claim 18, wherein the carrier is a pharmaceutically acceptable carrier.

16-17. (canceled)

18. (previously presented) A composition of matter comprising:

a) a purified polypeptide, said polypeptide comprising a non-naturally occurring vascular endothelial cell growth factor (VEGF) variant of native VEGF wherein said variant differs from native VEGF in that said variant contains at least one modification in the Kinase domain region (KDR) and/or FMS-like Tyrosine Kinase region (FLT-1), said modification(s) resulting in a modification of the binding affinity of said region(s) with respect to binding affinity of KDR and/or FLT-1 receptor(s) relative to the binding affinity of native VEGF; and

b) a carrier.

19-33. (canceled)

34. (currently amended) A composition comprising:

a) an isolated polypeptide, the polypeptide comprising a non-naturally occurring variant of vascular native endothelial cell growth factor (VEGF) wherein the variant comprises at least one modification in the Kinase domain region (KDR) and/or FMS-like Tyrosine Kinase region (FLT-1), the modification(s) resulting in a modification of the binding affinity of the region(s) with respect to binding affinity of KDR and/or FLT-1 receptor(s) relative to the binding affinity of native VEGF; and

b) a carrier.

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**Amendments to the Claims:**

This listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1-14. (canceled)

2 ~~15~~. (previously presented) The composition of matter of Claim ~~15~~<sup>1</sup>, wherein the carrier is a pharmaceutically acceptable carrier.

16-17. (canceled)

~~18~~. (currently amended) A composition of matter comprising:

a) a purified polypeptide, said polypeptide comprising a ~~non-naturally occurring~~ vascular endothelial cell growth factor (VEGF) variant of native VEGF wherein said variant differs from native VEGF in that said variant contains at least one non-conservative amino acid substitution~~modification~~ in the Kinase domain region (KDR) and/or FMS-like Tyrosine Kinase region (FLT-1), said ~~substitution~~~~modification~~(s) resulting in a modification of the binding affinity of the VEGF variant for said region(s) with respect to binding affinity of KDR and/or FLT-1 receptor(s) relative to the binding affinity of native VEGF for FLT-1 and/or KDR~~receptor(s); and~~

b) a carrier.

19-33. (canceled)

3 ~~34~~. (currently amended) A composition comprising:

a) an isolated polypeptide, the polypeptide comprising a variant of vascular native endothelial cell growth factor (VEGF) wherein the variant comprises at least one modification~~non-conservative amino acid substitution~~ in the Kinase domain region (KDR) and/or FMS-like Tyrosine Kinase region (FLT-1), the ~~substitution~~~~modification~~(s) resulting in a modification of the binding affinity of the VEGF variant for region(s) with respect to binding affinity of KDR

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and/or FLT-1 receptor(s) relative to the binding affinity of native VEGF for FLT-1 and/or KDR receptor(s); and

b) a carrier.

<sup>4</sup>  
~~35~~. (previously presented) The composition of claim <sup>3</sup>~~34~~, wherein the carrier is a pharmaceutically acceptable carrier.

<sup>7</sup>  
~~36~~. (previously presented) The composition of claim <sup>3</sup>~~34~~, wherein the polypeptide comprises one or more amino acid changes in the FLT-1 region comprising amino acids 60 to 70 of native VEGF.

<sup>8</sup>  
~~37~~. (previously presented) The composition of claim <sup>3</sup>~~34~~, wherein the polypeptide comprises one or more amino acid changes in the KDR region comprising amino acids 78 to 95 of native VEGF.

<sup>9</sup>  
~~38~~. (previously presented) The composition of claim <sup>3</sup>~~34~~, wherein one or more of amino acids 63, 64, 67, 82, 84, or 86 of native VEGF are ~~modified~~substituted.

<sup>11</sup>  
~~39~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 63 of native VEGF is ~~modified~~substituted.

<sup>12</sup>  
~~40~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 64 of native VEGF is ~~modified~~substituted.

<sup>13</sup>  
~~41~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 67 of native VEGF is ~~modified~~substituted.

<sup>14</sup>  
~~42~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 82 of native VEGF is ~~modified~~substituted.

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<sup>15</sup>  
~~43~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 84 of native VEGF is ~~modified~~substituted.

<sup>16</sup>  
~~44~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acid 86 of native VEGF is ~~modified~~substituted.

<sup>17</sup>  
~~45~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acids 63, 64, and 67 of native VEGF are ~~modified~~substituted.

<sup>18</sup>  
~~46~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acids 82, 84, and 86 of native VEGF are ~~modified~~substituted.

<sup>19</sup>  
~~47~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein amino acids 63, 64, 67, 82, 84, and 86 of native VEGF are ~~modified~~substituted.

<sup>10</sup>  
~~48~~. (currently amended) The composition of claim <sup>9</sup>~~38~~, wherein the amino acid ~~modification~~substitution is substitution by alanine.

49-59. (canceled)

<sup>5</sup>  
~~60~~. (new) The composition of claim <sup>3</sup>~~34~~, wherein the binding affinity of the VEGF variant for FLT-1 is less than the binding affinity of native VEGF for FLT-1.

<sup>6</sup>  
~~61~~. (new) The composition of claim <sup>3</sup>~~34~~, wherein the binding affinity of the VEGF variant for KDR is less than the binding affinity of native VEGF for KDR.

<sup>10</sup>  
~~62~~. (new) The composition of claim <sup>17</sup>~~45~~, wherein the amino acid substitution comprises D63A, E64A, and E67A.

<sup>21</sup>  
~~63~~. (new) The composition of claim <sup>9</sup>~~38~~, wherein the amino acid substitution comprises D63K.

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<sup>22</sup>  
~~64.~~ (new) The composition of claim <sup>21</sup>~~63~~, wherein the amino acid substitution comprises D63K, E64R, and E67K.

<sup>23</sup>  
~~65.~~ (new) The composition of claim <sup>17</sup>~~45~~, wherein the amino acid substitution comprises E64N and L66S.

<sup>24</sup>  
~~66.~~ (new) The composition of claim <sup>18</sup>~~46~~, wherein the amino acid substitution comprises R82E, K84E, and H86E.

<sup>25</sup>  
~~66.~~ (new) The composition of claim <sup>18</sup>~~46~~, wherein the amino acid substitution comprises R82A, K84A, and H86A.

<sup>26</sup>  
~~66.~~ (new) The composition of claim <sup>8</sup>~~37~~, wherein the amino acid substitution comprises R82N, I83L, and K84S.